Functional Genomics Initiative to Map Cellular Behavior

Opportunity

Recent developments in genome-scale DNA sequencing, high-throughput analytical tools (Figure 1), and computing technology have made feasible the genome-wide analysis of biomolecular function. It is now conceivable that complete functional maps of cellular behavior can be constructed, and strategies for modulating cellular activities can be formulated, with tremendous potential for advancing environmental management, human health, and economic productivity.

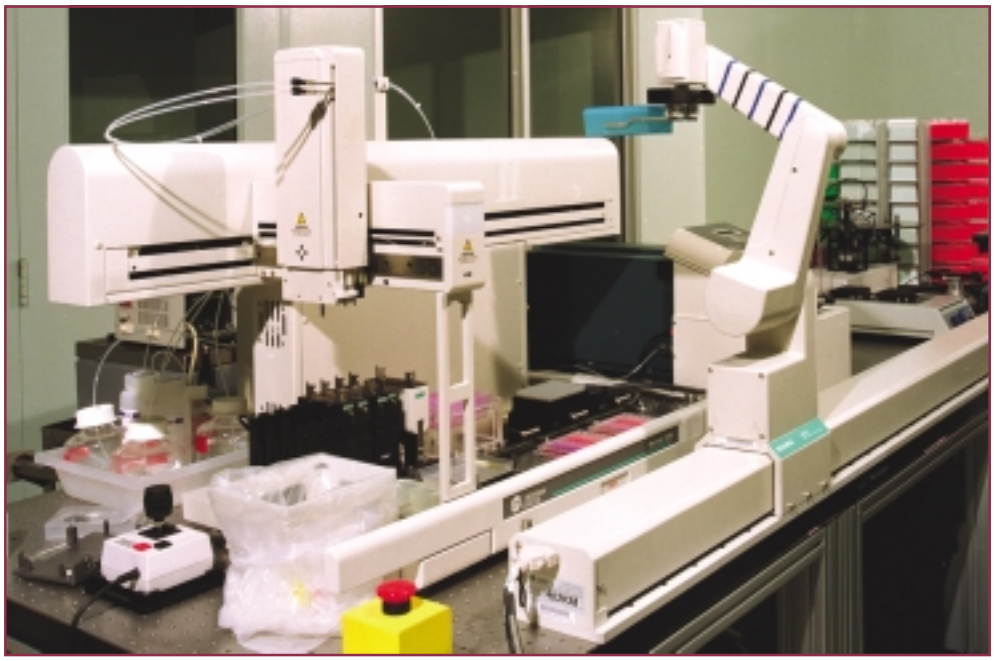

Figure 1. Robotics will be used to perform high-throughput molecular biology and biochemistry procedures.

Argonne's Strategy

Functional genomics aims to determine how genes and their products work and are regulated. Argonne proposes to undertake large-scale functional characterizations of macromolecules and macromolecular complexes (sometimes characterized as "molecular machines") to construct complete functional maps of cellular behavior.

The Functional Genomics Initiative will create the resources needed for mapping by developing high-throughput biochemical and biophysical techniques, as well as bioinformatics. When coordinated with Argonne's ongoing efforts in structural genomics, researchers will be able to support a set of experimental and computational strategies of sufficient diversity to support reliable genome-wide analyses of biomolecular function.

Applications

The combination of structural biology and high-throughput mapping of intermolecular interactions and informatics will also provide a huge database of protein/protein interactions and protein/small molecule interactions, leading to a better understanding of molecular recognition. This understanding will have broad implications for developing hybrid organic/inorganic materials, as well as new chemical, biological, and assembly processes for producing nanostructures. Argonne's multidisciplinary initiative in functional genomics is designed to support the U.S. Department of Energy's (DOE's) Biological and Environmental Research "Genomes to Life" program. This initiative also attracts co-sponsorship from DOE's Office of Basic Energy Sciences and the National Institutes of Health.

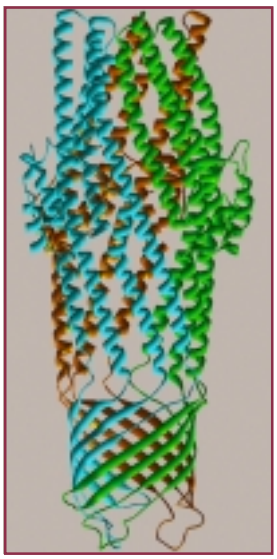

Figure 2. Data obtained by means of the SBC 191D beamline were used to determine the structure of transmembrane transport membrane TOL-C protein.

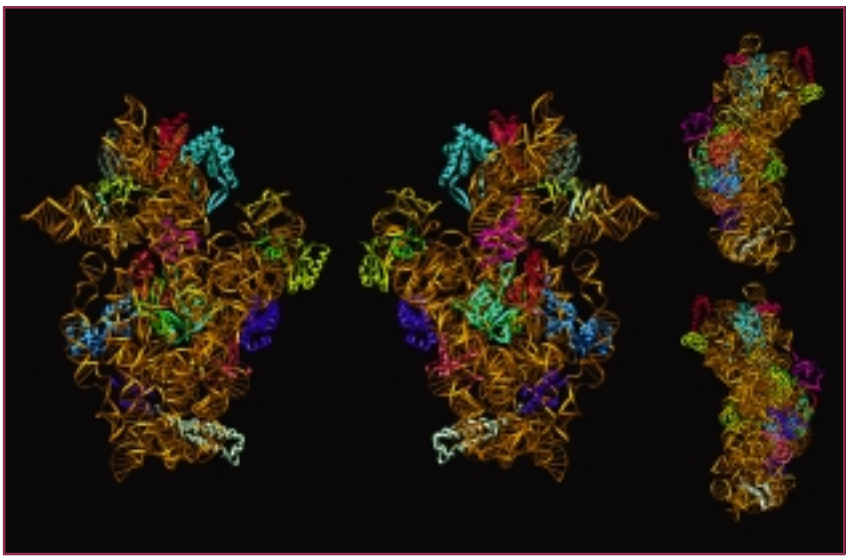

Figure 3. Structure of ribosome subunit was determined using the SBC 19ID beamline.

The structural biology component of Argonne's Functional Genomics Initiative is dependent on the crystallographic resources of the Laboratory's Structural Biology Center (SBC), which is funded by DOE. The SBC is one of the best facilities in the world for collecting high-resolution data from crystals of macromolecules and macromolecular complexes (Figures 2 and 3). The proposed high-throughput biochemistry component of the initiative builds on resources for high-throughput cloning, expression, and purification of proteins currently being developed in the Midwest Center for Structural Genomics (MCSG). In addition, the initiative's informatics component will encompass computational structural biology, genome, and proteome databases.

Collaborators

The University of Chicago
Northwestern University
University College, London
University of Texas
University of Toronto
University of Virginia
Washington University

Sponsors

U.S. Department of Energy, Office of Biological and Environmental Research and Office of Basic Energy Sciences; National Institutes of Health

Contact

Lee Makowski
Director, Biosciences Division
Phone: 630/252-3819
Fax: 630/252-3853
lmakowski@anl.gov